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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/294,663
Filing Date	April 19, 1999
First Named Inventor	Granados
Group Art Unit	1636
Examiner Name	Ibrahim, M.
Total Number of Pages in This Submission	
Attorney Docket Number	BTI-39CIP

ENCLOSURES *(check all that apply)*

- [x] Fee Transmittal Form
  - [x] Fee Attached
- [ ] Amendment / Response
  - [ ] After Final
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition Checklist and Accompanying Petition
- [ ] To Convert a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [x] Appeal Communication to Group (*Appeal Notice, Brief, Reply Brief*)
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Additional Enclosure(s) *(please identify below)*:

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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Brown & Michaels, PC
Signature	Thomas T. Aquilla
Date	4/20/01 Thomas T. Aquilla, 43,473

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date: 7099340000124715898 1

Typed or printed name	Theresa M. Rimbey		
Signature	Theresa M Rimbey	Date	4/20/01

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PTO/SB/17 (09-00)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2001

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT ($) 155.00

Complete if Known	
Application Number	09/294,663
Filing Date	4/19/99
First Named Inventor	Granados
Examiner Name	Ibrahim, M.
Group Art Unit	1636
Attorney Docket No.	BTI-39CIP

METHOD OF PAYMENT

1. ☑ The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:
   - Deposit Account Number: 02-0910
   - Deposit Account Name: Brown & Michaels PC
   - ☑ Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17
   - ☑ Applicant claims small entity status. See 37 CFR 1.27
2. ☑ **Payment Enclosed:** ☑ Check ☐ Credit card ☐ Money Order ☐ Other

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	710	201	355	Utility filing fee	
106	320	206	160	Design filing fee	
107	490	207	245	Plant filing fee	
108	710	208	355	Reissue filing fee	
114	150	214	75	Provisional filing fee	

SUBTOTAL (1) ($) 0.00

2. EXTRA CLAIM FEES

	Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =	X	=
Independent Claims		- 3** =	X	=
Multiple Dependent				=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	80	202	40	Independent claims in excess of 3
104	270	204	135	Multiple dependent claim, if not paid
109	80	209	40	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0.00

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	390	216	195	Extension for reply within second month	
117	890	217	445	Extension for reply within third month	
118	1,390	218	695	Extension for reply within fourth month	
128	1,890	228	945	Extension for reply within fifth month	
119	310	219	155	Notice of Appeal	
120	310	220	155	Filing a brief in support of an appeal	155.00
121	270	221	135	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,240	241	620	Petition to revive - unintentional	
142	1,240	242	620	Utility issue fee (or reissue)	
143	440	243	220	Design issue fee	
144	600	244	300	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Petitions related to provisional applications	
126	240	126	240	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	710	246	355	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	710	249	355	For each additional invention to be examined (37 CFR § 1.129(b))	
179	710	279	355	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 155.00

SUBMITTED BY				Complete *(if applicable)*	
Name (Print/Type)	Thomas T. Aquilla	Registration No. (Attorney/Agent)	43,473	Telephone	607-256-2000
Signature	Thomas T. Aquilla			Date	4/20/01

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS

April 20, 2000

In re Application of:	Granados *et al.*
Serial No.	09/294,663
Filed:	April 19, 1999
For:	A NOVEL INVERTEBRATE INTESTINAL MUCIN cDNA AND RELATED PRODUCTS AND METHODS
Examiner:	Ibrahim, M.
Art Unit:	1638
Attorney Docket No.:	BTI-39-CIP

APPEAL BRIEF

HONORABLE COMMISSIONER OF
PATENTS AND TRADEMARKS
Washington, D.C. 20231

Sir:

This application is before the Honorable Board of Appeals on appeal from the Final Rejection by the Examiner dated December 12, 2000, wherein claims 1, 6 and 9 were finally rejected.

(1)
REAL PARTY IN INTEREST

An assignment of the invention claimed in this application from the Appellant to Boyce Thompson Institute for Plant Research, Inc., a State of New York corporation, is recorded in

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited in the U.S. Postal Service as Certified Mail No: 70993400001247158981 with a return receipt requested, in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 on April 20, 2001.

Theresa M. Rimbey

Theresa M. Rimbey

0235. Accordingly, the Real Party in Interest is Boyce Thompson Institute for Plant Research, Inc.

(2)
RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to Appellant, the Appellant's legal representative, or Assignee, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

(3)
STATUS OF CLAIMS

Claims 1, 3, 5-7, 9-10 and 20-22 are pending in the application; claims 2, 4, 8 and 11-19 were canceled. Claims 3, 5, 7, 10 and 20-22 are allowed. Claims 1, 6 and 9 stand finally rejected.

The Final Rejection of claims 1, 6 and 9 is appealed. The Claims on Appeal are set forth in the Appendix to this brief.

(4)
STATUS OF AMENDMENTS AFTER FINAL REJECTION

No amendments were filed after the Final Office Action of December 12, 2000.

(5)
SUMMARY OF THE INVENTION

The present invention represents the disclosure of a novel insect intestinal mucin (IIM) and the identification of numerous closely related IIM proteins. The IIM protein of *Trichoplusia ni* was identified and cloned, and its cDNA and amino acid sequences are disclosed. The IIM DNA and protein molecules are useful for the production of recombinant

vectors and transgenic plants, wherein said transgenic plant is the product of an insertion of a gene expression vector including a DNA molecule that encodes an IIM protein, such that an engineered host cell comprising the IIM DNA molecule is capable of expressing an IIM protein. The current invention also provides for the use of purified and recombinant IIM proteins. Using the knowledge of the proteinaceous components of the peritrophic membrane disclosed in the application, and particularly the IIM proteins, it is possible to enhance the effectiveness of bio-engineered pesticides, recombinant viral vectors, and enhance the defenses of transgenic plants susceptible to attack by phytophagous invertebrate organisms.

For example, using IIM DNA molecules, it is possible to prepare an IIM protein or peptide by transforming any host cell with an expression vector comprising a promoter operatively linked to a nucleotide sequence which codes for an IIM protein, culturing the host cell under conditions such that the IIM protein is expressed, and purifying the IIM protein from the host cells. In addition, using the information disclosed in the application, one can construct a recombinant plant that expresses an IIM protein or antibodies to disrupt peritrophic membrane function and formation in phytophagous invertebrate pests, such as plant-chewing insects.

(5A)

References Relied Upon by the Examiner

The Final Rejections of claims 1, 6 and 9 are made under 35 U.S.C. § 112, first paragraph, and, as such, the Examiner does not rely upon any prior art references in the Final Rejection of the claims.

(6)

ISSUES

1. Is the specification enabling under 35 U.S.C. § 112, first paragraph, for claims 1, 6 and 9?

2. Does the specification provide an adequate written description under 35 U.S.C. § 112, first paragraph, for claims 1, 6 and 9?

(7)
GROUPING OF CLAIMS

Claims 1, 6 and 9 are argued as a group, and thus stand or fall together. The claims on appeal are set forth in the Appendix to this brief.

Independent claim 1 is a composition of matter claim directed to a transformed plant, wherein the novel feature is a gene encoding an invertebrate intestinal mucin (IIM) protein. Independent claim 6 is a method claim directed to a method for producing a protein by transformation of and expression in a host cell, wherein the point of novel lies in a gene encoding an invertebrate intestinal mucin (IIM) protein. Claim 9 depends from claim 6 and includes the additional limitation that the expression vector further comprises a transfer molecule. Claims 1, 6 and 9 thus all have in common the novel feature of a gene encoding an IIM protein, and are therefore argued as a group.

(8)
ARGUMENTS

(8A)
The Specification Enables One of Ordinary Skill in the Art to Make and Use the Invention of Claims 1, 6 and 9

Claims 1, 6 and 9 stand finally rejected under 35 U.S.C. § 112, first paragraph, as not being enabled by the specification. Appellant disagrees and respectfully requests that this Board reverse the rejection.

The issue is whether undue experimentation would be required for one of ordinary skill in the art to make and use the invention of claims 1, 6 and 9, broadly drawn to any transformed plant comprising any gene encoding an invertebrate intestinal mucin (IIM) protein, and a method for expressing any IIM protein by transforming any host cell with an expression vector comprising a promoter operatively linked to a nucleotide sequence encoding a protein of any IIM, in light of the teachings of the disclosure and what was known in the prior art as of June 24, 1998, the effective filing date of Appellant's patent application.

The Patent Office argues that the specification is not enabling for any transformed plant comprising any gene encoding an invertebrate intestinal mucin (IIM) protein, and a method for producing any IIM protein by transforming any host cell with an expression vector comprising a promoter operatively linked to a nucleotide sequence encoding a predetermined protein of any IIM, and a dependent method further including an expression vector comprising a glutathione-S-transferase gene. More particularly, the Patent Office maintains the Final Rejection of claims 1, 6 and 9 on the grounds that the claims are broadly drawn to any transformed plant comprising a gene encoding any IIM protein, and methods for producing and recovering said protein by transformation of any host cell. See Final Office Action of December 12, 2000 at page 2, paragraph 3, through page 3.

The Patent Office asserts that the claims are over broad on the grounds that "No guidance has been presented for the isolation of other invertebrate intestinal genes encoding IIM proteins with chitin binding activity and their potential as an insecticide in the exemplified and non-exemplified host cells. Furthermore, genes encoding proteins thought to be directly involved in disease resistance may be ineffective in conferring disease resistance, following their expression in transgenic plants (*see e.g.*, Linthorst *et al.*, page 285, Abstract). Expression of insecticidal proteins in transformed plants may fail to confer protection (*see e.g.*, Dandekar *et al.*, page 151, Abstract)." Office Action of February 8, 2000, page 4, line 21 through page 5, line 4.

The Patent Office further asserts that "the specification fails to provide an[y] sic evidence that the antibody obtained for the *T. ni* protein will also be terribly specific to the other IIM proteins covered by the instant claims. No guidance has been provided for the obtention of specific probes, hybridization and wash conditions for the exemplified or non-exemplified genes encoding functional IIM proteins or antibodies to the IIM proteins, and it is not clear if any has been isolated from other invertebrates at the time of Applicant's invention." Final Action of December 12, 2000, page 3, lines 5-10.

Essentially, the Patent Office maintains that undue experimentation would be required for those of ordinary skill in the art to make and use the IIM protein of any species, because Appellant's application discloses as working examples the DNA and polypeptide sequences of only two (2) isoforms of IIM isolated from one insect species, *Trichoplusia ni*. Hence, the Patent Office asserts that the broad claims are not enabled by the disclosure, on the grounds

that the art is unpredictable and the specification does not provide sufficient guidance, particularly considering the small number of working examples described.

Similarly, in regard to the transformation of plants and other types of host cells, the Patent Office maintains that undue experimentation would be required to practice the broadly claimed invention, because Appellant's application discloses as a preferred embodiment only one prophetic example of a transgenic plant that expresses IIM-IgG, whereas the number of different plants and other organisms that fall within the scope of the claims is extremely large. Apparently, the Patent Office also doubts that Appellant's invention is operative.

The Law: Enablement

All questions of enablement are evaluated against the claimed subject matter. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (C.C.P.A. 1971). The focus of the examination inquiry is whether the subject matter within the scope of the claim is enabled. In re Fisher, 427 F.2d 833, 166 USPQ 18, 24 (C.C.P.A. 1970).

The test for enablement is whether the disclosure, when originally filed, contained sufficient information regarding the subject matter of the claims as to enable those of ordinary skill in the pertinent art to make and use the invention. The standard is whether the experimentation necessary to practice the invention is undue or unreasonable. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). *See also* U.S. v. Telectronics, Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.") (emphasis added). A patent need not teach, and preferably omits, what is well known in the art. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies , Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. In re Certain Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*, Massachusetts Institute of Technology v. A.B. Fortia, 774 F.2d 1104, 227 USPQ 428 (Fed.

Cir. 1985). *See also* In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. Thus, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (C.C.P.A. 1976).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement).

In Wands, the court noted that there was no disagreement as to the facts, but merely a disagreement as to the interpretation of the data and the conclusion to be made from the facts. In re Wands, 858 F.2d at 736-40, 8 USPQ2d at 1403-07. The Court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed;" and "all of the methods needed to practice the invention were well known." 858 F.2d at 740, 8 USPQ2d at 1406. After considering all the factors related to the enablement issue, the court concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." Id., 858 F.2d at 740, 8 USPQ2d at 1407.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). However, the determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. In

re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors, while ignoring one or more of the others. The Examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of non-enablement must be based on the evidence as a whole. Id., 858 F.2d at 740, 8 USPQ2d at 1407.

(8A1)
Enablement Must Be Determined Against the Claimed Subject Matter

All questions of enablement are evaluated against the claimed subject matter. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (C.C.P.A. 1971). The focus of the examination inquiry is whether the subject matter within the scope of the claim is enabled. In re Fisher, 427 F.2d 833, 166 USPQ 18, 24 (C.C.P.A. 1970).

In support of the Final Rejection of claims 1, 6 and 9, the Patent Office asserts that "No guidance has been presented for the isolation of other invertebrate intestinal genes encoding IIM proteins with chitin binding activity and their potential as an insecticide in the exemplified and non-exemplified host cells. Furthermore, genes encoding proteins thought to be directly involved in disease resistance may be ineffective in conferring disease resistance, following their expression in transgenic plants (*see e.g.*, Linthorst *et al.*, page 285, Abstract). Expression of insecticidal proteins in transformed plants may fail to confer protection (*see e.g.*, Dandekar *et al.*, page 151, Abstract)." Office Action of February 8, 2000, page 4, line 21 through page 5, line 4. The Patent Office further asserts that "the specification fails to provide an[y] sic evidence that the antibody obtained for the *T. ni* protein will also be terribly specific to the other IIM proteins covered by the instant claims. No guidance has been provided for the obtention of specific probes, hybridization and wash conditions for the exemplified or non-exemplified genes encoding functional IIM proteins or antibodies to the IIM proteins, and it is not clear if any has been isolated from other invertebrates at the time of Applicant's invention." Final Action of December 12, 2000, page 3, lines 5-10.

Claim 1 is directed to a transformed plant comprising a gene encoding an invertebrate intestinal mucin (IIM) protein, such that the plant is capable of expressing the IIM protein. Claims 6 and 9 are directed to a method of producing an IIM protein by transforming and culturing a host cell under conditions such that the IIM protein is expressed. The subject

matter of claims 1, 6 and 9 does not include the features of chitin binding, insecticidal activity or disease resistance, and does not encompass IIM antibodies or antibody genes. See Claims On Appeal in the Appendix to this brief. Thus, no teaching in regard to chitin binding, insecticidal activity, disease resistance or IIM antibodies is necessary to enable those of ordinary skill in the art to make and use the invention of claims 1, 6 and 9. The Appellant is under no duty to provide any disclosure regarding chitin binding, insecticidal activity, disease resistance or IIM antibodies, because such features are clearly outside the scope of claims 1, 6 and 9. Therefore, the Patent Office's arguments regarding these features are irrelevant to the patentability of the claims.

Furthermore, it is respectfully submitted that the Patent Office is erroneous in its assertion that the specification does not provide guidance for the isolation of other IIM proteins, or any evidence regarding the specificity of the *T. ni* IIM protein antibody, and its assertion that it is not clear if any other IIM proteins have been isolated from other invertebrates at the time of the invention. As discussed in detail below, the specification provides ample guidance to direct one of ordinary skill in the art in the identification and isolation of IIM proteins from other species. More particularly, the specification expressly discloses the use of the *T. ni* IIM antibody for the identification of IIM and IIM-like proteins in at least 18 different invertebrate species, in addition to *T. ni*.

(8A2)
Undue Experimentation is Not Needed to Make and Use the Claimed Invention

ANALYSIS OF THE WANDS FACTORS

The Examiner's analysis must consider all the evidence related to each of the Wands factors, and any conclusion of non-enablement must be based on the evidence as a whole. In re Wands, 858 F.2d at 740, 8 USPQ2d at 1407. However, in the Final Rejection of claims 1, 6 and 9, the Patent Office confines its analysis to the breadth of the claims, predictability in the art, and the level of guidance provided by the applicant, while ignoring the remaining Wands factors. It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the Wands factors, while ignoring one or more of the others. Id., 858 F.2d at 740, 8 USPQ2d at 1407 (emphasis added). Further, as noted above, most of the Patent

Office's arguments are either irrelevant to the enablement of the claimed subject matter, or unsupported by the facts of record, as explained below.

a. Breadth of the claims and nature of the invention

Claim 1 is directed to any transformed plant comprising a gene encoding any invertebrate intestinal mucin (IIM) protein, such that the plant is capable of expressing the IIM protein. Claims 6 and 9 are directed to a method of producing any IIM protein by transforming and culturing any host cell under conditions such that the IIM protein is expressed. The invention involves the genetic engineering of plants and other organisms, and the identification, isolation and *in vitro* expression of proteins. It is undisputed that the claims are broad generic claims directed to transgenic plants and methods of expressing IIM proteins in any host, and the nature of the invention is biological and complex.

b. State of the prior art, level of skill and level of predictability in the art

The identification and cloning of genes and the transformation of various host cell types for the expression of foreign proteins is a mature art that has developed into a multi-billion dollar industry. The art is highly advanced, and has become increasingly predictable and reliable. Since 1983, when the first transgenic plant was disclosed, the art has become much more predictable, and reliable methods have been developed for the transformation of virtually all types of plants, as well as other organisms. In particular, since 1996, transgenic plant varieties have constituted an increasingly large percentage of several major US staple crops, and the expression of foreign proteins in various cultured cells has been widely practiced in the chemical and pharmaceutical industries for several years. Thus, the state of the art, level of skill and predictability in the art at the time of the invention were all high.

c. Level of guidance provided by inventor and existence of working examples

A patent need not teach, and preferably omits, what is well known in the art. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). The specification discloses the DNA and protein sequences of two IIM proteins isolated from *T. ni*, and the identification of IIM and IIM-like proteins in a total of eighteen (18) other insect species from five (5) different orders. Furthermore, all of the methods needed to practice the invention are well known in the art. In its patent application, Appellant discloses numerous resources

providing detailed descriptions of all the well known methods needed to practice the invention, including the identification and cloning of genes, transformation of various host cell types, including plants and other organisms, and the expression of foreign proteins. Specification at page 42, line 16 to page 45, line 29. Thus, contrary to the Patent Office's assertion, there is ample direction and guidance in the specification for one of ordinary skill in the art to practice the claimed invention.

d. Quantity of experimentation needed based on the content of the disclosure

The invention involves the genetic engineering of plants and other organisms, and the identification, isolation and *in vitro* expression of proteins. Clearly the experimentation needed to practice the invention is extensive and quite complicated, as it requires complex genetic manipulations and the biosynthesis of macromolecules in useful quantities. Typically, such experiments require extensive time, relatively large, sophisticated manufacturing facilities, and a large amount of highly skilled labor. However, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. In re Certain Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*, Massachusetts Institute of Technology v. A.B. Fortia, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). *See also* In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404.

Indeed, such complex, laborious, time-consuming experimentation is typical in the art, and the methods needed to make and use the invention are routine in the art and are widely practiced on an industrial scale. The disclosure cites numerous resources providing detailed descriptions of all the well known methods needed to practice the invention, including the identification and cloning of genes, transformation of various host cell types, including plants and other organisms, and the expression of foreign proteins. Specification at page 42, line 16 to page 45, line 29.

Moreover, the specification expressly discloses the use of the *T. ni* IIM antibody for the identification of IIM and IIM-like proteins in at least 18 different invertebrate species, in addition to *T. ni*. Specification at Table 3 and page 31, line 15 to page 33, line 33. "These studies have demonstrated that mucin (IIM) or mucin-like PM proteins are present in a wide variety of insect species in 5 orders." Specification at page 33, lines 24-25. Thus, based on

the content of the disclosure and the fact that the art typically engages in complex experimentation, the quantity of experimentation needed to practice the invention is not undue.

e. The evidence regarding the Wands factors must be considered as a whole

The determination that undue experimentation would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The Examiner's analysis must consider all the evidence related to each of the Wands factors, and any conclusion of non-enablement must be based on the evidence as a whole. Wands, 858 F.2d at 740, 8 USPQ2d at 1407.

CONCLUSION

The Patent Office clearly did not consider all of the Wands factors. Based on the foregoing analysis of all of the Wands factors, it is evident that Appellant provides considerable direction and guidance in the specification, that the state of the prior art, level of skill and predictability in the art were high at the time the application was filed, that all of the methods needed to practice the invention were well known in the art, and that the quantity of experimentation needed to practice the invention was not undue. Therefore, considering the evidence as a whole, Appellant's specification is enabling with respect to the claims at issue. In re Wands, 858 F.2d at 740, 8 USPQ2d at 1406.

Accordingly, Appellant respectfully requests that this Board reverse the rejection of claims 1, 6 and 9 under 35 U.S.C. § 112, first paragraph, for lack of enablement, in view of the above remarks.

(8B)
The Disclosure Conveys That The Inventor Had Possession of the Invention of Claims 1, 6 and 9

Claims 1, 6 and 9 stand finally rejected under 35 U.S.C. § 112, first paragraph, as not being supported by an adequate written description. Appellant disagrees and respectfully requests that this Board reverse the rejection.

The issue is whether the specification reasonably conveys to one of ordinary skill in the art that the patent applicant invented any transformed plant comprising any gene encoding an invertebrate intestinal mucin (IIM) protein, and a method for expressing any IIM protein by transforming any host cell with an expression vector comprising a promoter operatively linked to a nucleotide sequence encoding a protein of any IIM, as of June 24, 1998, the effective filing date of Appellant's patent application. In this case, the determination hinges on whether Appellant's disclosure of the nucleotide and polypeptide sequences of IIM14 and IIM22, isolated from *T. ni*, and the identification of IIM and IIM-like proteins from at least eighteen (18) other species from five (5) orders of insects describes structural features common to the members of the genus, which features constitute a substantial portion of the genus. *See* Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Patent Office argues that the specification does not reasonably convey to one of ordinary skill in the art that the applicant had possession of any transformed plant comprising any gene encoding an invertebrate intestinal mucin (IIM) protein, and a method for producing any IIM protein by transforming any host cell with an expression vector comprising a promoter operatively linked to a nucleotide sequence encoding a predetermined protein of any IIM, . More particularly, the Patent Office maintains the Final Rejection of claims 1, 6 and 9 on the grounds that the claims are broadly drawn to any transformed plant comprising a gene encoding any IIM protein, and methods for producing and recovering said protein by transformation of any host cell. See Final Office Action of December 12, 2000 at page 4.

The Patent Office asserts that the claims are over broad on the grounds that "the specification only provides guidance for a cDNA sequence from *Trichoplusia ni* in a vector encoding *Trichoplusia ni* IIM protein." Office Action of February 8, 2000, page 5, lines 18-19. The Patent Office cites Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991) at page 1021, in support of its argument that "a gene or promoter is not reduced to practice until the inventor can define it by "its physical and chemical properties" (*e.g.*, a DNA sequence)" and page 1027, in support of its argument that "the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof." Office Action of February 8, 2000, page 6, second paragraph (emphasis added).

The Patent Office further cites Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997), in support of its argument that "a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism." Office Action of February 8, 2000, page 6, third paragraph.

Finally, the Patent Office asserts that the claims are drawn to a multitude of genes "encoding a multitude of functional IIM proteins of undefined physical and structural characteristics" and "given the lack of written description as stated above, a mere cross-reaction of an antiserum to *T. ni* IIM protein with proteins from 18 other insect species will not envisage a person skilled in the art that the applicant has possession of the genes of the invention as broadly claimed. See, the Synopsis of Application of Written Description Guidelines made available at the USPTO web site March 1, 2000. See, also, Amgen Inc and university of California disclosed in page 6 of the last office action." Final Office Action of December 12, 2000 at page 4, third paragraph.

Essentially, the Patent Office maintains that specification does not reasonably convey to one of ordinary skill in the art that the patent applicant invented the IIM protein of any species, because Appellant's application discloses as working examples the DNA and polypeptide sequences of only two (2) isoforms of IIM isolated from one insect species, *Trichoplusia ni*. Hence, the Patent Office asserts that the broad claims are not supported by the written description, on the grounds that a gene or promoter is not reduced to practice until the inventor can define it by "its physical and chemical properties," particularly considering the small number of working examples described, and its conclusion that a "mere cross-reaction of an antiserum to *T. ni* IIM protein with proteins from 18 other insect species will not envisage a person skilled in the art that the applicant has possession of the genes of the invention as broadly claimed."

The Law: Written Description

The test for compliance with the written description requirement is whether the Appellants' disclosure as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or

absence of literal support in the specification for the claim language. Ralston Purina Co. v. Far-Mar-Co., Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (*quoting* In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983). The standard is whether the written description allows persons of ordinary skill in the art to recognize that the patent applicant invented what is claimed. In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. However, the subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. *See* In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983). Further, the disclosure must be read in light of the knowledge of those skilled in the art, as evidenced by references available to the public prior to the filing date. In re Lange, 644 F.2d 856, 863, 209 USPQ 288, 294 (C.C.P.A. 1981).

The description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or by means of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) (emphasis added). *See also* the Patent Office's Synopsis of Application of Written Description Guidelines, made available at the USPTO web site March 1, 2000, at: http://www.uspto.gov/web/menu/pats.html.

(8B1)
The Specification Conveys to One of Ordinary Skill in the Art That the Applicant Invented What Is Claimed

In support of the Final Rejection of claims 1, 6 and 9, the Patent Office argues that "the specification only provides guidance for a cDNA sequence from *Trichoplusia ni* in a vector encoding *Trichoplusia ni* IIM protein." Office Action of February 8, 2000, page 5, lines 18-19. The Patent Office further asserts that "a gene or promoter is not reduced to practice until the inventor can define it by "its physical and chemical properties" (*e.g.*, a DNA sequence)" and that "the disclosure of a few gene sequences did not enable claims broadly

drawn to any analog thereof." Office Action of February 8, 2000, page 6, second paragraph (emphasis added). The Patent Office further asserts that "a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein." Office Action of February 8, 2000, page 6, third paragraph. Finally, the Patent Office asserts that the claims are drawn to a multitude of genes "encoding a multitude of functional IIM proteins of undefined physical and structural characteristics" and "a mere cross-reaction of an antiserum to *T. ni* IIM protein with proteins from 18 other insect species will not envisage a person skilled in the art that the applicant has possession of the genes of the invention as broadly claimed." Final Office Action of December 12, 2000 at page 4, third paragraph.

Claim 1 is directed to a transformed plant comprising a gene encoding an invertebrate intestinal mucin (IIM) protein, such that the plant is capable of expressing the IIM protein. Claims 6 and 9 are directed to a method of producing an IIM protein by transforming and culturing a host cell under conditions such that the IIM protein is expressed. The subject matter of claims 1, 6 and 9 does not encompass analogs of IIM proteins or DNA molecules. See Claims On Appeal in the Appendix to this brief. Further, the issue of enablement has been addressed already, and the rejection currently at hand is for lack of a sufficient written description. Thus, the Patent Office's argument regarding the enablement of claims broadly drawn to an analog of IIM proteins or DNA molecules and the citation of Amgen at page 1027 are irrelevant to whether the written description provides sufficient support for the claimed invention.

In regard to the Patent Office's argument that a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism, and the citation of Regents of the University of California, the facts in the present case clearly distinguish it from Regents. In Regents, the critical fact was that the patent applicant disclosed only the protein sequence of a gene and a method for obtaining a cDNA. The applicant did not disclose the identification of multiple cDNAs encoding the protein or, more importantly, the identification of numerous similar proteins, as in the present case. Thus, the disclosure in Appellant's application of multiple *T. ni* IIM cDNA sequences, as well as the identification of numerous IIM and IIM-like proteins in other species distinguishes the present case. Note, however, that Regents is applicable to the facts in the present case, in support of the proposition that "the description of

a genus of cDNAs may be achieved by .... means of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Further, it is respectfully submitted that the Patent Office is erroneous in its assertion that the specification only provides guidance for a cDNA sequence from *Trichoplusia ni*, and that "a mere cross-reaction" of an antiserum to *T. ni* IIM protein with proteins from 18 other insect species would not convey to one of ordinary skill in the art that the applicant had possession of the genes of the invention as broadly claimed. Appellant's disclosure substantially defines the essential physical and structural features that characterize IIM proteins, and constitutes the disclosure of a representative number of species from within the claimed genus, as explained in detail below. Furthermore, as discussed above, and further below, the specification provides ample guidance to direct one of ordinary skill in the art in the identification and isolation of IIM proteins from other species More particularly, the specification expressly discloses the use of the *T. ni* IIM antibody for the identification of IIM and IIM-like proteins in at least 18 different invertebrate species, in addition to *T. ni*. Specification at Table 3 and page 31, line 15 to page 33, line 33. "These studies have demonstrated that mucin (IIM) or mucin-like PM proteins are present in a wide variety of insect species in 5 orders." Specification at page 33, lines 24-25.

Finally, the Patent Office is erroneous in its assertion that the claims are drawn to a multitude of genes encoding a multitude of functional IIM proteins of "undefined physical and structural characteristics". Substantial physical and chemical structural attributes of IIM proteins, sufficient to clearly distinguish them from other proteins, are disclosed in the patent application. More particularly, the IIM proteins have an amino acid composition similar to that of a typical vertebrate mucin, being a secreted epithelial mucin rich in threonine, serine, proline, alanine and glycine, and low in aromatic amino acids, and exhibiting the characteristics of high glycosylation, high resistance to protease, stability over a wide pH range, and the presence of strong intermolecular sulfide bonds. The IIM proteins in particular further are characterized by localized expression in the midgut of invertebrates, chitin binding activity and strong association with the peritrophic membrane, and specific binding with the IIM antibody. Specification at page 7, line 3 to page 8, line 25, and page 11, line 3 to page 14, line 22.

(8B2)
The Application Describes a Representative Number of Species From Within the Claimed Genus

In support of the Final Rejection of claims 1, 6 and 9, the Patent Office argues that a gene or promoter is not reduced to practice until the inventor can define it by "its physical and chemical properties (*e.g.*, a DNA sequence)." The Patent Office further argues that the specification only provides guidance for a cDNA sequence from *Trichoplusia ni* in a vector encoding *Trichoplusia ni* IIM protein, stating that a "mere cross-reaction" of an antiserum to *T. ni* IIM protein with proteins from 18 other insect species would not convey to one of ordinary skill in the art that the applicant had possession of the genes of the invention as broadly claimed.

The subject matter of a claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. *See* In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983). More particularly, a sufficient written description of a genus of cDNAs may be achieved by means of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Further, the disclosure must be read in light of the knowledge of those skilled in the art, as evidenced by references available to the public prior to the filing date. In re Lange, 644 F.2d 856, 863, 209 USPQ 288, 294 (C.C.P.A. 1981).

Patent Office policy appears to comport with Regents, as the Patent Office Written Description Guidelines also state quite clearly that "The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus." Patent Office's Synopsis of Application of Written Description Guidelines at page 31, paragraph 3, and page 31, paragraph 4 to page 32, *citing* Regents, 43 USPQ2d at 1406. *See generally* Synopsis of Application of Written Description Guidelines, made available at the USPTO web site March 1, 2000, at: http://www.uspto.gov/web/menu/pats.html.

The issue is whether Appellant's disclosure of the nucleotide and polypeptide sequences of IIM14 and IIM22, isolated from *T. ni*, and the Appellant's identification of IIM

and IIM-like proteins from at least eighteen (18) other species from five (5) orders of insects describes structural features common to the members of the genus, sufficient to distinguish the claimed proteins. In the present case, the specification discloses numerous structural features common to members of the claimed genus. Indeed, substantial physical and chemical structural attributes of IIM proteins, sufficient to clearly distinguish them from other proteins, are disclosed in the patent application. More particularly, the IIM proteins have an amino acid composition similar to that of a typical vertebrate mucin, being a secreted epithelial mucin rich in threonine, serine, proline, alanine and glycine, and low in aromatic amino acids, and exhibiting the characteristics of high glycosylation, high resistance to protease, stability over a wide pH range, and the presence of strong intermolecular sulfide bonds. The IIM proteins in particular further are characterized by localized expression in the midgut of invertebrates, chitin binding activity and strong association with the peritrophic membrane, and specific binding with the IIM antibody. Specification at page 7, line 3 to page 8, line 25, and page 11, line 3 to page 14, line 22.

A review of the full content of Appellant's specification reveals that the essential feature of the invention of claims 1, 6 and 9 is an IIM protein having the foregoing structural features. The specification discloses the use of an IIM-specific antibody to identify numerous members of the IIM protein genus. The clones so identified were not sequenced, however, several were shown to encode proteins of the expected molecular weight and bind very strongly to the IIM antibody. A person of ordinary skill in the art would not expect substantial variation among the species encompassed within the scope of the claims, because the highly specific binding of the IIM antibody would be expected to yield structurally similar proteins. The foregoing structural features of IIM, which are common to members of the claimed genus, constitute a "substantial portion" of the claimed genus. Thus, Appellant's patent application discloses a representative number of species from within the claimed genus, since the high specificity of the IIM antibody in combination with the coding function of the DNA and the level of skill and knowledge in the art are sufficient to determine that the patent applicant was in possession of the invention of claims 1, 6 and 9.

Accordingly, Appellant respectfully requests that this Board reverse the rejection of claims 1, 6 and 9 under 35 U.S.C. § 112, first paragraph, for lack of a sufficient written description, in view of the above remarks.

(9)
CONCLUSION

In view of the arguments set forth in this brief, Appellant respectfully requests that this Board reverse the rejections of claims 1, 6 and 9 under 35 U.S.C. § 112, first paragraph, and allow the application and pending claims to issue.

(10)
ADDITIONAL COMMENT AND RESERVATION

Appellant believes it has responded to all of the reasons for rejection which it can discern in the Office Action. However, Appellant reserves the right to respond with a supplementary argument to any reasons for rejection which were not responded to in this brief, if the Examiner should assert in his Answer that any were not responded to herein.

Respectfully submitted:

By: Thomas T. Aquilla

Thomas T. Aquilla, Reg. No. 43,473, Attorney for Appellant
Brown & Michaels, P.C.
400 M&T Bank Building
118 North Tioga Street
Ithaca, NY 14850
Telephone: (607) 256-2000
Fax: (607) 256-3628
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APPENDIX

Claims on Appeal

1. A transformed plant, comprising an expression vector, wherein said expression vector comprises a gene encoding an invertebrate intestinal mucin (IIM) protein operably linked to an expression control sequence, such that said transformed plant is capable of expressing said IIM protein.

6. A method of producing a IIM protein or peptide comprising:

a) transforming a host cell with an expression vector comprising a promoter operatively linked to a nucleotide sequence which codes for a predetermined protein or peptide of a IIM protein;

b) culturing said host cell under conditions such that said IIM protein is expressed in recoverable quantity;

c) lysing said host cell; and

d) recovering said IIM protein.

9. The method of claim 6 wherein said expression vector further comprises a gene encoding a transfer molecule such as glutathione-S-transferase.